

IN THE UNITED STATES DISTRICT COURT  
FOR THE DISTRICT OF DELAWARE

CADENCE PHARMACEUTICALS, INC.  
and SCR PHARMATOP,

Plaintiffs,

vs.

C.A. No. 11-733-LPS

PADDOCK LABORATORIES, INC.;  
PERRIGO COMPANY;  
PADDOCK LABORATORIES, LLC;  
EXELA PHARMA SCIENCES, LLC;  
EXELA PHARMSCI, INC.; and  
EXELA HOLDINGS, INC.,

Defendants.

**DECLARATION OF DR. SREE RAMA MURTHY MALLIPEDDY REGARDING THE  
HYPERTONICITY OF CERTAIN EXAMPLES IN U.S. PATENT 6,028,222**

I, Sree Rama Murthy Mallipeddy, Ph.D., declare as follows:

1. I am Chief Scientific Officer of Exela Pharma Sciences, LLC.—one of the Exela entities in this litigation.
2. I have been Chief Scientific Officer of Exela Pharma Sciences, LLC. from about 2009.
3. Prior to my current position, I was Executive Director of Exela Pharma Sciences Private Limited from about 2004.
4. I hold a Bachelor's, Master's, and Ph.D. in Pharmaceutical Sciences from Andhra University, Visakhapatnam, India.
5. I also hold a post graduate diploma in Applied Statistics from the same university.

6. After completing my education in 1985, I have held research and development, quality control, quality assurance, and management positions with increasing responsibility at several pharmaceutical companies.

7. Over the course of my career, I have routinely calculated the tonicity of numerous pharmaceutical formulations.

8. I have evaluated the tonicity of certain formulations disclosed in the examples of United States Patent 6,028,222 (“the ‘222 patent”).

9. The tonicity calculations that I performed are based on the sodium chloride equivalents method as described in: Poon, “Tonicity, Osmoticity, Osmolality, and Osmolarity,” Remington: The Science and Practice of Pharmacy, 21st ed., Ch. 18, 250-265, 2006 (attached as Exhibit 1 to this declaration).

10. A pharmaceutical formulation for injection is considered isotonic (i.e., having the same osmotic pressure as that of body fluids) if it exerts osmotic pressure equivalent to that of a 0.9% sodium chloride solution (Exhibit 1 at 250, 252).

11. The osmolarity (a measure of osmotic pressure) of an isotonic solution of 0.9% sodium chloride is approximately 290 mOsmol/L. (Exhibit 1 at 252).

12. Solutions with greater osmolarity than approximately 290 mOsmol/L are considered hypertonic and those with lesser osmolarity are hypotonic. Neither such non-isotonic solution is recommended for administration directly into a peripheral vein. (Exhibit 1, at 252).

13. Hypertonic solutions must be diluted before direct administration into a peripheral vein. (Exhibit 1, at 257).

14. Several formulations presented in the ‘222 patent are hypertonic, using the sodium chloride equivalents method described in Exhibit 1.

15. The osmolarity contribution of just the solvents used to dissolve the acetaminophen in Examples 3.1, 5.1, 6.1, 7.1 and at col. 5, ll. 37-55, is shown in the Table below:

Solvent	Composition per mL	Calculated Osmolarity (mOsmol/L)
Polyethylene glycol 400	0.360 mL (406 mg) [40.6% w/v]	$(40.6 * 292) / 8.5 = 1395$
Propylene glycol	0.270 mL (279.7 mg) [27.0%w/v]	$(27.0 * 292) / 2.0 = 3942$
		<b>Total: 5337</b>

16. The osmolarity contribution of other ingredients (i.e., acetaminophen, pH adjuster, etc) dissolved in the Examples will add to the total osmolarity of the Table above.

17. Based on Exhibit 1 and the above calculations, the total osmolarity of the formulations disclosed in the Examples 3.1, 5.1, 6.1, 7.1 and at col. 5, ll. 37-55 of the '222 patent must exceed by several fold even the most extreme tolerable limits mentioned in Exhibit 1 at 252, namely, about 800 mOsmol/L. Therefore, these formulations are hypertonic and must be diluted before they can be administered to a patient by an intravenous route.

I declare under penalty of perjury that the foregoing facts are true and accurate.

Executed on May 9, 2013

 5/9/2013

Sree Rama Murthy Mallipeddy, Ph.D.

**CERTIFICATE OF SERVICE**

I, Pilar G. Kraman, hereby certify that on May 10, 2013, I caused to be electronically filed a copy of the foregoing document with the Clerk of the Court using CM/ECF, which will send notification that such filing is available for viewing and downloading to the following counsel of record:

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I further certify that on May 10, 2013, I caused a true and correct copy of the foregoing document to be served by e-mail on the above-listed counsel of record and on the following:

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Dated: May 10, 2013

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/s/ Pilar G. Kraman

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